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10/532,412	04/22/2005	Akifumi Okuda	0425-1185PUS1	9129

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EXAMINER	
SHAHNAN SHAH, KHATOL S	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/532,412	OKUDA ET AL.	
	Examiner	Art Unit	
	Khatol S. Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) *2,4,6 and 7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/04/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

1. The amendment and response filed 12/08/2008 have been entered into the record. Claims 1 and 5 have been cancelled. Claims 1-7 are pending. Claims 1, 3 and 5 are under examination. Claims 2, 4, 6 and 7 have withdrawn from consideration as being drawn to non-elected inventions. Specification multiple paragraphs have amended.

Information Disclosure Statement

2. Applicants' information disclosure statement of 11/04/2008 is acknowledged. The references have been considered by the examiner. See attached 1449.

Objections Withdrawn

3. Objection to the specification in regard to an embedded hyperlink and/or other form of browser-executable code, made in paragraph 4 of the office action mailed February 6, 2008 is withdrawn in view of applicants' amendments filed 12/08/2008.

Rejections Maintained

Double Patenting

4. Rejection of claims 1, 3 and 5 based on a judicially created obvious type double patenting made in paragraph 10 of the office action mailed February 6, 2008 is maintained.

The rejection was stated below:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3 and 5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 24 of copending Application No.11/213,962. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of both applications are drawn to production of a macrolide compound or its derivative by a biological transformation method using Streptomyces species. The formula II and I of claim 1 of the instant application and the formula 2 and 3 of Application No.11/213,962 are variant of each other because claim 1 of Application No.11/213,962 recites that the R group on those formula is hydroxy , acetoxy or methoxy. Claim 24 of Application No.11/213,962 recites that culturing *Streptomyces sp.* Mer 11107, FERM p-18144 or its variants can be used to obtain the claimed compound or its derivative.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants' arguments of December 08, 2008 have been fully considered but they are not persuasive.

- The applicant argues: The invention disclosed in claims 1 and 24 of application Serial No. 11/213,962 requires a fermentation step to obtain 11107B or 11107D. However, the reference application fails to disclose or suggest hydroxylation (-OH) of the fermentation product at the 16-position. The presently claimed invention includes production of a macrolide compound 1 I107D of formula (II) having a hydroxyl (OH) group at the 16-position, starting from a macrolide compound 11107B of formula (I) which has no hydroxyl (OH) group at the 16-position. The presently claimed production is performed by incubation with a microorganism. Claims 1 and 24 of the reference application fail to show 11107B used as a starting material and also fails to show 11107B being hydroxylated at the 16-position by means of a microorganism. Accordingly, withdrawal of the double patenting rejection is in order and is earnestly solicited.

In response to the applicants' argument, it is the office position that claims 1 and 24 of Application No.11/213,962 does not recite a fermentation step furthermore claim 1 of Application No.11/213,962 recites that the R group on those formula is **hydroxy,** acetoxy or methoxy. Claim 24 of Application No.11/213,962 recites that culturing *Streptomyces sp.* Mer 11107, FERM p-18144 or its variants can be used to obtain the claimed compound or its derivative.

Claim Rejections - 35 USC § 102

5. Rejection of claims 1, 3 and 5 under 35 U.S.C. 102(b) as being anticipated by Asai et al. (Mizui et al.) (WO 02/0600890A1), made in paragraph 13 of the office action mailed August 08, 2008 is maintained.

The rejection was stated below:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the

United States.

Note: As mentioned in the previous action, acknowledgment is made of applicants' claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. Japan 2002-346796, filed on 11/29/2002. However, no translation of said application has been filed. For the purpose of prior art the priority date will be granted as the filing date of PCT application of 11/27/2003.

Claims 1, 3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Asai et al. (Mizui et al.) (WO 02/0600890A1). Prior art of record applicants' 1449.

Claims are drawn to a method of producing a macrolide compound 11107D from a macrolide compound 11107B by a biological transformation method comprising the steps of:

a) contacting compound 11107B with genus *Streptomyces*;

b) incubating the mixture; and

c) collecting compound 11107D from the mixture.

Asai et al. (Mizui et al.) teach a method of producing a macrolide compound 11107D from a macrolide compound 11107B by a biological transformation method comprising the steps of:

a) contacting compound 11107B with genus *Streptomyces*;

b) incubating the mixture; and

c) collecting compound 11107D from the mixture. (see column 37, column 38, and lines 33-68, and column 39, lines 1-40).

Asai et al. (Mizui et al.) teach 11107B (see pages 5 and 67 and 72) 11107D (see pages 5 and 67 and 75) , conversion of 111107B to 1107D biological transformation or bioconversion (see abstract), *Streptomyces* Mer -11107 FERM P-1844 or its mutants) (see preparation). Since FERM BP-8551 strain characteristics is unknown, the strain has not been disclosed. Therefore it is determined that the strain of *Streptomyces* used by Asai et al. is identical to the strain recited in claim 5 since the required bioconversion is achieved by the strain of Asai et al. The prior art teaches the claimed invention.

Applicants' arguments of December 08, 2008 have been fully considered but they are not persuasive.

- However, Mizui et al. fails to disclose a method of producing macrolide 11107D by incubating a bacterial strain belonging to the genus Mortierella, the genus Streptomyces or the family Micromonosporaceae with the macrolide of 11107B. *(See,* Mizui et al., at paragraph [0274]). That is- while Mizui et al. may disclose 11107B and ll107D - Mizui et al. do not disclose *how to synthesize 111071)from 11107B using a bacteria,* as required by Applicants' claims.

In response to the applicants' argument, it is the office position that firstly the claims are reciting a method of producing the macrolide compound without reciting specific method steps. The claims are drawn to a product by a process and the product is known, secondly Mizui et al. do disclose a method of producing macrolide 11107D by incubating a bacterial strain belonging to the genus Mortierella, the genus Streptomyces or the family Micromonosporaceae with the macrolide of 11107B. Mizui et al., at paragraph [0274] as applicants point out recites" Further, the present invention provides the production process of the compound of the present invention, **a pharmacologically acceptable salt thereof or a hydrate** of them, which comprises culturing Streptomyces sp. Mer. 11107, FERM P-18144 or its variant in a nutrient culture medium, collecting the compounds described in any of the above are from the culture solution, and **carrying out various modification synthesis by using the obtained compounds as a starting material to obtain derivatives thereof."** Emphasize added to the fact that carrying out various modification synthesis by using the obtained compounds as a starting material to obtain derivatives thereof.

Claim Rejections - 35 USC § 103

6. Rejection of claims 1, 3 and 5 under 35 U.S.C. 103(a) as being unpatentable by Seki-Asano et al., made in paragraph 14 of the office action mailed August 08, 2008 is maintained.

The rejection was stated below:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable by Seki-Asano et al. (The Journal of Antibiotics, vol. 47, No. 12, pp. 1395-1401, 1994).

Claims are drawn to a method of producing a macrolide compound 11107D from a macrolide compound 11107B by a biological transformation method comprising the steps of:

a) contacting compound 11107B with genus *Streptomyces*;

b) incubating the mixture; and

c) collecting compound 11107D from the mixture.

Seki-Asano et al. teach isolation and characterization of a new 12- membered macrolide FD-895 with a basic structure recited in figure 1 which is produced from by biological transformation from a culture of *Streptomyces hygroscoicus* A-9561. The instant claims read on the method and compound which is taught by the reference. The reference teach the basic structure of the claimed formulas I and II.

Since FERM BP-8551 strain characteristics is unknown, the strain has not been disclosed. Therefore it is determined that the strain of *Streptomyces* used by Seki-Asano et al. is identical to the strain recited in claim 5 since the required bioconversion is achieved by the strain of Seki-Asano et al.

It would be *prima facie* obvious to one of the ordinarily skilled in the art to replace the methyl group at the position 16 of the FD-895 to a hydroxyl group to obtain compound 11107D of formula II. Production and substitution of methyl or hydroxyl group in the same scaffold in a family of known antibiotic compounds will be considered as optimization of assay parameters.

Applicants' arguments of December 08, 2008 have been fully considered but they are not persuasive.

- Seki-Asano's FD-895 is significantly different from Applicants' 11107B and 11107D, having a hydroxyl group in the 17-position and having a methoxy group in the 21 - position. FD-895 differs from 11107B in having no hydroxyl group at the 16-position. FD-895 is obtained directly from a medium of *Streptomyces hygroscoicus* A-9561. See Seki-Asano, page 1395, lines 11-12 from the bottom. The Seki-Asano reference provides no teaching relevant to biological hydroxylation of a particular compound at a particular position. No motivation to or rationale for hydroxylation of 11107B at position 16 is provided by the Seki-Asano reference in particular or by the prior art in general. The Seki-Asano reference fails to show 11107B used as a starting material and also fails to show a microorganism being used to hydroxylate a particular compound at a particular position (much less, 11107B at the 16-position) and also fails to show 11107D being obtained as a final product. Seki-Asano fails to suggest that *Streptomyces hygroscoicus* A-9561 can be used to bioconvert 11107B to I 1107D by hydroxylation at the 16-position.

In response to the applicants' argument, it is the office position that the motivation for hydroxylation of 11107B at position 16 is provided by one of the ordinarily skilled in the art to replace the methyl group at the position 16 of the FD-895 to a hydroxyl group to obtain compound 11107D of formula II. Production and substitution of methyl or hydroxyl group in the same scaffold in a family of known antibiotic compounds is

considered as optimization of assay parameters and will be well within reach of one skilled in the art.

Status of Claims

7. No claims are allowed.

Conclusion

8. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is 571-272-0863. The examiner can normally be reached on Monday-Friday 7:30 AM-5:00 PM If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Khatol S Shahnan-Shah/
Examiner, Art Unit 1645
February 23, 2009
/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645